PATENT COOPERATION TREATY

PCT

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference R 42991	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2004/000162	International filing date *(day/month/year)* 13.01.2004	Priority date *(day/month/year)* 14.01.2003
International Patent Classification (IPC) or national classification and IPC C07K14/47, A61K38/08		
Applicant MATTNER, Frank		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
10.08.2004	09.05.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Mandl, B Telephone No. +49 89 2399-8434

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/000162

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-21 as originally filed

   Claims, Numbers

   1-9 as originally filed

   Drawings, Sheets

   1/5-5/5 as originally filed

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-9
Industrial applicability (IA)	Yes:	Claims	1-9
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☒ furnished subsequently to this Authority for the purposes of search and/or examination

   ☒ received by this Authority as an amendment on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Re Item V.

The following documents are referred to in this communication:

D1: WO 00/72880 A (NEURALAB LTD); December 2000

D2: REINEKE U ET AL: "Identification of distinct antibody epitopes and mimotopes from a peptide array of 5520 randomly generated sequences" JOURNAL OF IMMUNOLOGICAL METHODS, vol. 267, no. 1, pages 37-51; 1 September 2002

Article 33(3) PCT

i. The present application does not meet the criteria of **Article 33(1) PCT**, because the subject matter of claims 1-9 does not involve an inventive step in the sense of **Article 33(3)PCT** for the following reasons:

ii. Document **D1** is considered to represent the most relevant state of the art. It discloses the use of N-terminal fragments of Aβ42 in a vaccine for Alzheimer's disease (AD). According to D1, N-terminal fragments of 2-20 residues are preferred over the intact Aβ42 because they provide a useful immunogenic response, they do not generate an immunogenic response against APP, they are simple to manufacture and they do not aggregate in the same manner as intact Aβ42 (D1: page 14, lines 19-29). D1 finally proposes to use mimetics (mimotopes) of Aβ42 as therapeutic agents (D1: page 16, lines 26-29).

iii. In the light of D1, the problem to be solved by the present application is the making of the mimotopes as proposed in D1 in order to improve the available Aβ42 vaccine for Alzheimer disclosed in D1.

iv. The methodology for the production of mimotopes was known to the skilled person. The applicant himself mentions the disclosures made by **D2** as the basis for the making of the mimotopes.

v. The subject-matter of claims 1-5 and 9 lacks an inventive step because the incentive to make mimotopes was clearly derivable from D1 and the actual making of the

mimotopes required known technology only.

vi. This inventivity objection is based on the fact that the claims have a very broad scope, and therefore comprise many types of compounds with various features. Consequently, for such a scope, the demonstration of an unexpected or surprising effect is impossible because, as it can be seen on page 19 of the present application (table 1) and on page 21 (table 2), already the 21 different peptides tested show a range of inhibitory capacity from none to strong. This also means that peptides are comprised in the scope of the claims which do not solve the problem posed.

vii. However, it appears as if the present application describes peptides which, indeed, show an unexpected or surprising effect, i.e. strong inhibitory capacity. For such specific peptides, an inventive step could be acknowledged.

viii. With regard to claim 6 the following is communicated: As described in the present application, antibodies which are specific for Aβ but do not recognize APP were known in the art. From D1 it was already known that the vaccine should be based on N-terminal fragments because they do not generate an immunogenic response against APP. Consequently, the selection of an antibody specific for DAEFRH appears obvious and is not considered to make the method of claim 6 inventive in the light of documents D1 (which proposes to look for mimotopes) and D2 (which discloses the method). Dependent claims 7 and 8 only relate to features which are well known in the art and, therefore, cannot be used to overcome the inventive step objection directed against claim 6. Thus, claims 7 and 8 also lack an inventive step.

Re Item VI.

Document EP1361349, published on 12.11.2003, claims an earlier priority than the present application. The applicant is informed that, in the European phase, this document may become relevant for novelty aspects.

Re Item VIII.

Finally, it is communicated that the scope of claims 1-5 is broader than justified by the description because, as it can be seen from Tables 1 and 2, only some of the plurality of peptides claimed show in fact an inhibitory capacity, i.e. can be used for the preparation of a vaccine for AD (**Article 6 PCT**).